Pharmacotherapy Update

WINTER 2014-2015 LEBANON VAMC

INSIDE THIS ISSUE:

A Note from the Editors

2014 has already come to an end, but there were plenty of exciting things that happened at the end of the year.
This edition of the newsletter features a literature review on the new National Lipid Association Guidelines. These guidelines reintroduce the concept of treating to LDL goals.

We move along to the Drug Information Corner to find an article written by Quoc Vo, who is a 2015 Pharm.D. candidate from Wilkes University, that features *Afrezza*®, inhaled insulin.

Next up is an article from our very own, Jennifer James. After being asked by a provider about the cautions of prescribing testosterone, she researched an answer to share with all of us. You can learn more about the signs and symptoms of androgen deficiency and learn about what the risks are and who is at an increased risk of having adverse events.

In the last issue, we said our good-byes to Grazyna. This time, we're welcoming in the New Year and a new addition to our pharmacy team! Take a minute to learn a little bit more about Robi, our newest pharmacy technician, and look at his adorable son. Awww!

You can then go on to find that there was a newly initiated best practice tablet-splitting auto conversion for potassium chloride. Thank you to our PGY1 pharmacy residents for working on this cost-savings initiative with the help of Paul and Kevin, during their administration block.

We close out this issue of the newsletter with some Pharmacy Phun. On the last page you can test your knowledge of pharmacy trivia and also check out some great pharmacy pick up lines. *Disclosure*: The pick up lines in this article are not guaranteed to get you a date for Valentine's Day, only a good laugh!

We hope you have a safe and warm winter as well as a happy, healthy new year!

Christina Inteso, Pharm.D.
Dina Hunsinger-Norris, Pharm.D., BCPS, AQ Cardiology

To Treat to Target or Not to Treat to Target?

By: Chelsea Fitzgerald, Pharm.D.

In fall 2014, the National Lipid Association (NLA) countered the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines by releasing their own set of guidelines for the management of dyslipidemia. The NLA guidelines more closely resemble the ATP3 guidelines and brought the return of the "treat-to-target" approach for managing dyslipidemia. To date, only the executive summary of Part 1 of the guidelines has been published, which includes the classification of lipid levels, targets for intervention, atherosclerotic cardiovascular disease (ASCVD) risk assessment and treatment goals based on risk, and the use of lifestyle and drug therapies to reduce morbidity and mortality.

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Drug Information Corner

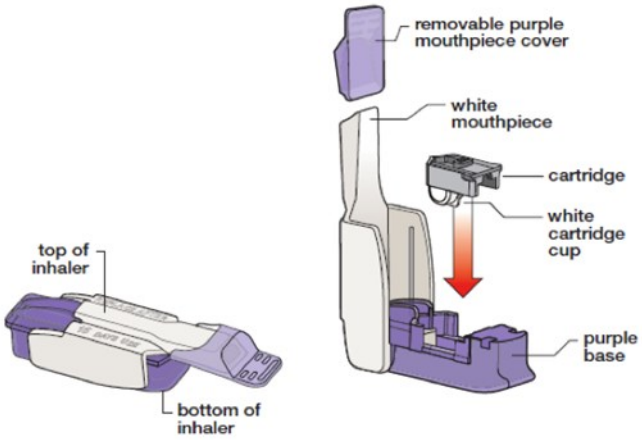
Inhaled Insulin: Afrezza®

Quoc Duy Vo, Pharm.D. Candidate 2015

Type 2 Diabetes (T2DM) is one of the most common diseases in America. According to the Centers for Disease Control and Prevention (CDC) 2014 statistics, 9.3% of the population has diabetes, and 25.9% patients with diabetes are 65 years or older. Insulin is a pancreatic hormone that is secreted by beta cells of the islets of Langerhans to metabolize glucose. Human insulin injections were approved by the FDA in 1982 and are now used worldwide. The first inhaled insulin (Exubera®) from Pfizer was approved by the FDA in January 2006. There were many issues with this medication including the high cost, bulky inhaler, and concerns about adverse effects on lung function. Therefore, less than 1% of patients on insulin used Exubera®, and it was withdrawn from the market in October 2007.

Afrezza® is an insulin powder inhaler that was approved by the FDA in June of 2014 and is manufactured by Mannkind Corporation. It is the only ultra rapid-acting human insulin on the market, and has faster pharmacokinetic and pharmacodynamic properties than the three rapid-acting insulin analogs, aspart, glulisine, and lispro. Just like rapid acting insulin injections, Afrezza® is administered before each meal to control prandial blood glucose levels.[2]

Know your AFREZZA® inhaler:



Indication: It has been approved for type 1 and 2 diabetes mellitus. It is not used instead of long-acting insulin and must be used with long-acting insulin in patients with type 1 diabetes.

Efficacy: A randomized controlled-trial compared Afrezza® to insulin aspart in 3,017 type 1 and 2 patients over a 24 week period. The mean reduction in HbA1C in the Afrezza® group was 0.4%, which is non-inferior to insulin aspart. However, a subgroup study compared Afrezza® plus oral anti-diabetic medications versus placebo in patients with T2DM and showed a significantly lower HbA1C with Afrezza®.[2]

Dose: Afrezza® is available as 4 unit or 8 unit cartridges. Insulin-naive patients start with 4 units at each meal. For patients previously on SubQ mealtime insulin, use the chart below:

Injected Mealtime Dose	Afrezza® dose
≤4 units	4 units
5 to 8 units	8 units
9-12 units	12 units
13-16 units	16 units
17-20 units	20 units
21-24 units	24 units

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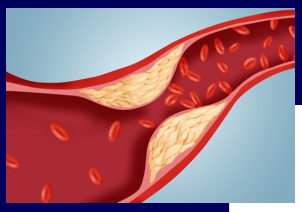


To Treat to Target or Not to Treat to Target? *Continued from page 1*

Part 2 of the guidelines is to include further elaboration on lifestyle therapies, the treatment of special populations, and strategies to assist with patient adherence.

The two primary targets of therapy recommended by the NLA include non-HDL (total cholesterol minus HDL cholesterol) and LDL. Non-HDL is recommended as the primary target over LDL because non-HDL testing is universally available, requires no additional cost, and can be obtained in a non-fasting state. Additionally, evidence has shown that non-HDL is more predictive of ASCVD risk than LDL and when non-HDL and LDL are discordant, ASCVD risk is more closely aligned with non-HDL. Lastly, the NLA guidelines are the first to introduce apolipoprotein B as an optional secondary target of therapy, once non-HDL and LDL are at goal. Studies have shown that apo B is strongly associated with ASCVD event risk, is more predictive of ASCVD risk than LDL, and is a potential contributor to lipoprotein-related residual risk, as it may remain elevated even when non-HDL and LDL are at goal.

Table 1 below summarizes the criteria for risk categorization along with the recommended treatment goals according to the NLA guidelines. As with previous guidelines, the NLA supports risk quantification for certain patients, particularly those that fall into the moderate risk category in order to assess if they should be considered as high risk. The NLA does not endorse a specific risk equation, and it provides definitions for high risk based on both the Framingham Risk Score and the Pooled Cohort Equation used in the ACC/AHA guidelines.

Table 1. Criteria for ASCVD risk assessment, treatment goals for atherogenic cholesterol, and levels at which to consider drug therapy

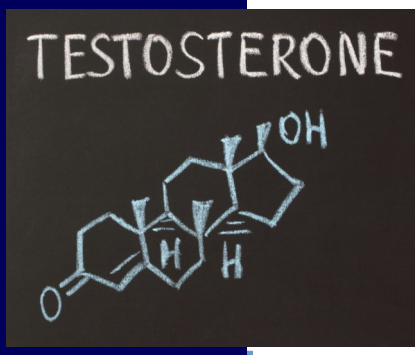
Risk Category	Criteria	Treatment Goal	Consider Drug Therapy
		Non-HDL-C mg/dL LDL-C mg/dL	
Low	0-1 major ASCVD risk factors Consider other risk indicators, if known	<130 <100	≥190 ≥160
Moderate	2 major ASCVD risk factors Consider quantitative risk scoring Consider other risk indicators	<130 <100	≥160 ≥130
High	≥3 major ASCVD risk factors Diabetes mellitus (type 1 or 2) 0-1 other major ASCVD risk factors, *and* No evidence of end organ damage CKD stage 3B or 4 LDL ≥ 190 mg/dL Quantitative risk score reaching high risk threshold	<130 <100	≥130 ≥100
Very High	ASCVD Diabetes mellitus ≥2 other major ASCVD risk factors, *or* End organ damage	<100 <70	≥100 ≥70

As for pharmacologic treatment of dyslipidemia, the NLA joins the consensus that statin therapy should be first-line. However, in contrast to the 2013 ACC/AHA guidelines, the NLA recommends the addition of combination therapy with non-statin medications if treatment goals are not achieved with statin monotherapy. The guidelines do not endorse one non-statin therapy over another, so it is left up to the patient and clinician to decide which treatment is best for the individual patient.

So what do you think? Should we be using whatever means necessary to get patient's to target cholesterol levels or is statin therapy enough to lower ASCVD risk?

Drug Information Corner

Jennifer M. James, Pharm.D.



Question: What are the cautions with prescribing testosterone?

Answer: Testosterone Replacement Therapy (TRT) is indicated in male hypogonadism, which is only diagnosed in men with consistent signs and symptoms **AND** low serum testosterone level.

Signs and Symptoms Suggestive of Androgen Deficiency in Men	
Specific	**Other, less specific**
• Incomplete or delayed sexual development (eunuchoidism) • ↓ sexual desire (libido) and activity • ↓ spontaneous erections • Breast discomfort (gynecomastia) • Loss of body hair (axillary and pubic), ↓ shaving • Very small (<5ml) or shrinking testes • Inability to father children, low or zero sperm count • ↓ height, low trauma fracture, low bone mineral density • Hot flashes, sweats	• ↓ energy, motivation, initiative, self-confidence • Feeling sad or blue, depressed mood, dysthymia • Poor concentration and memory • Sleep disturbances, ↑ sleepiness • Mild anemia (normochromic, normocytic, in the female range) • ↓ muscle bulk and strength • ↑ body fat (body mass index) • ↓ physical or work performance

An initial diagnostic test is done in the morning of total testosterone level by radioimmunoassay (RAI). This laboratory value is drawn in morning since serum testosterone levels exhibit a circadian variation that peaks in the morning. Total testosterone is the sum of unbound and protein-bound testosterone in circulation. Normative ranges vary among labs and assays, thus recommended to use lower limit of normal [Total testosterone level 280-300 ng/dl (9.8-10.4 nmol/l), Serum free testosterone 5-9 pg/ml (0.17-0.31 nmol/l)]. To confirm diagnosis, there must be a repeat low measurement of total testosterone level. It however is not recommended to confirm diagnosis during an acute or sub-acute illness as results may be skewed.

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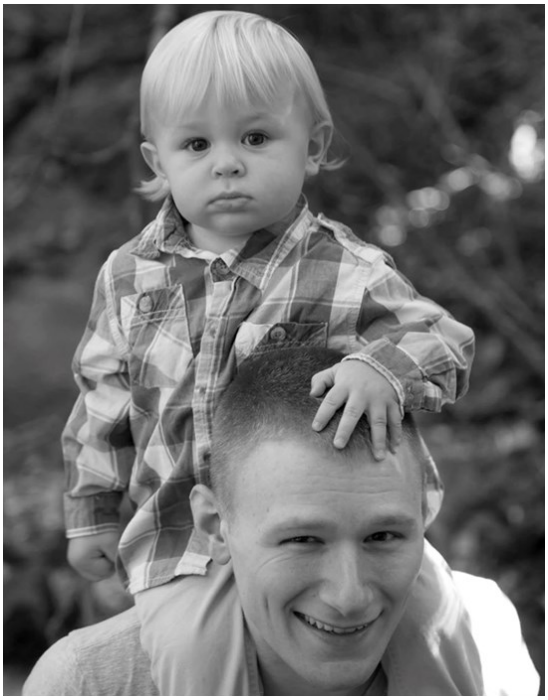
Tech Time Out: Robi Janoszek



I'm sure everyone has seen Robi working hard in the pharmacy by this point. But how much do you really know about him? Robi started working at the VA on November 17, 2014 as a pharmacy technician. Contrary to popular belief, he is not a student. Before joining us at the VA, he previously worked at the Wal-Mart pharmacy. He became interested in the field of pharmacy after his uncle, who is a pharmacist, suggested it to him. Robi is not a Pennsylvania native, but has been living in Lebanon since June of 2009. He is originally from Massapequa, NY. Outside of work, you can find Robi taking his son to the park or going camping in the summer. He also enjoys working out and building PC's.

Fun Facts:

- Favorite vacation destination: Clearwater, FL, but would like to see Miami
- Favorite winter activity: Skiing, but making hot cocoa and watching the snow fall is nice too
- If you could be on any TV show, which would you choose? The Walking Dead, because zombies and the apocalypse are fascinating!

Local P&T Update: Potassium Chloride Cost Savings Initiative

By: Christina Inteso, Jennifer James, Ambili Prasad, Janki Shah

The following policy is now in place after being passed at the November P&T Meeting. Previously, the pharmacy was dispensing both 10 mEq and 20 mEq tablets as whole tablets. It was determined that splitting the 20 mEq tablets is more cost effective than using the 10 mEq tablets. Therefore, patients that are currently on 10mEq tablets will automatically be converted to 20 mEq tablets which they will be required to split in half. All new 10 mEq prescriptions will be dispensed as 20 mEq tablets with directions of "take one-half tablet".

In keeping with current best practice tablet-splitting auto conversions, if a patient is unable to split tablets, a non-formulary request will need to be placed for the whole 10 mEq tablets. Current procedures for placing non-formulary requests will be followed. All providers were notified via email of this policy change.

Inhaled Insulin: Afrezza®

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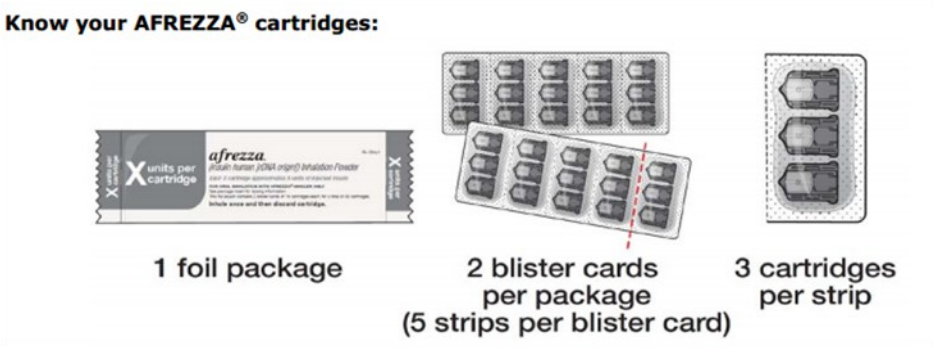
Safety: Afrezza® has a Black Box Warning for acute bronchospasm, especially in patients with asthma and COPD. Other common adverse reactions associated with Afrezza® found in clinical trials were hypoglycemia (67%), cough, and throat pain or irritation.[1]

- Lung cancer: During clinical trials, two cases were reported in patients with a history of heavy tobacco use. After completion of the trial, two additional cases were reported in nonsmokers. Due to lack of evidence, the use of inhaled insulin in patients with a history of, active, or risk of lung cancer should be avoided.
- Pulmonary lung function: Inhaled insulin may cause a decline in lung function measured by FEV_1. A clinical trial showed a decline within the first three months. This decline persisted, but did not worsen with continued therapy for up to 2 years. It is recommended to obtain pulmonary function tests at baseline and six months. If FEV_1 declines more than 20%, consider discontinuing therapy.[2]
- Smokers/recent cessation: Not recommended due to lack of data.

"Afrezza® has a Black Box Warning for acute bronchopasm"



Storage: Unopened package of single-use cartridges: Store at 2ºC to 8ºC (36°F to 46°F) until expiration date on package. If package is not refrigerated, contents must be used within 10 days. Unopened blister cards and strips must be used within 10 days and opened strips must be used within 3 days. Cartridges should be at room temperature for at least 10 minutes before administration. Inhaler may be stored in refrigerator but should be at room temperature prior to use. Inhaler should be replaced every 15 days to maintain drug delivery.[3]

References:

1. Micromedex. Insulin Human Inhaled. 2014.

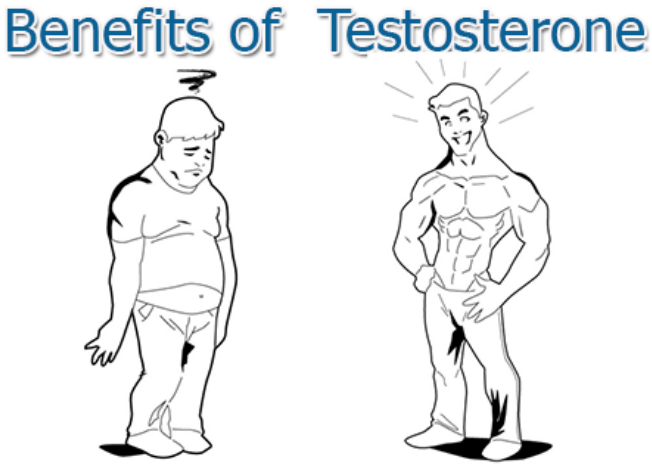
2. Fda.gov. FDA approves Afrezza to treat diabetes [Internet]. 2014 [cited 17 November 2014]. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm403122.htm

3.Afrezza [package Insert]. Mannkind Corp.;2014

Cautions with Testosterone (Continued from page 4)

Other warnings and precautions for testosterone products include the fact that testosterone is pregnancy risk factor X, a controlled substance (CIII), and contains a **U.S. BOXED WARNING** for Serious Pulmonary Oil Microembolism (POME). Reactions and anaphylaxis have been reported with testosterone injections which include: chest pain, urge to cough, dizziness, dyspnea, throat tightening, syncope, which may be life threatening. For that reason, it is recommended to monitor patients for 30 minutes after injection. The FDA also issued a General Warning in June 2014 for Venous Thromboembolism in association with testosterone products, and there was a Product Safety Alert, last updated February 2014, which indicated that the FDA is currently investigating risk of stroke, heart attack and death in men taking FDA-approved testosterone products. Thus, the Endocrine Society suggests it may be prudent to avoid testosterone therapy in men who have experienced a cardiovascular event (eg, MI, stroke, acute coronary syndrome) in the past 6 months.

Therapy not recommended:
Very high risk of serious adverse outcomes
• Metastatic prostate cancer • Breast cancer
Moderate to high risk of adverse outcomes
• Unevaluated prostate nodule or induration • Prostate specific antigen (PSA) 4 ng/ml (>3ng/ml in patients at high risk for prostate cancer such as African Americans or men with first-degree relatives with prostate cancer) • Hematocrit > 50% • Untreated severe obstructive sleep apnea • Uncontrolled or poorly controlled heart failure • Patients desiring fertility • Severe lower urinary tract symptoms associated with benign prostatic hypertrophy as indicated by the American Urological Association (AUA)/International Prostate Symptom Score (IPSS) >19



References:

1. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *The Endocrine Society*. https://www.endocrine.org/~/media/endosociety/Files/Publications/Clinical%20Practice%20Guidelines/FINAL-Androgens-in-Men-Standalone.pdf. Accessed November 6 2014.

2. FDA adding general warning to testosterone products about potential for venous blood clots. *FDA*. Available at http://www.fda.gov/Drugs/DrugSafety/ucm401746.htm. Accessed 6 2014.

3. FDA Drug Safety Communication: FDA evaluating risk of stroke, heart attack and death with FDA-approved testosterone products. *FDA*. Available at http://www.fda.gov/Drugs/DrugSafety/ucm383904.htm. Accessed 6 2014.

Pharmacy Phun!

Pharmacy Related Trivia

1.) What was the first state to require pharmacists to be licensed? And when?
   A. Pennsylvania, 1901
   B. New York, 1857
   C. Louisiana, 1806
   D. Alabama, 1814

2.) When and where was the first hospital pharmacy opened in the United States?
   A. 1798, New Jersey
   B. 1752, Pennsylvania
   C. 1847, Delaware
   D. 1873, Connecticut

3.) Before Charles S. Walgreen Sr. became a pharmacist, what did he do for a living?
   A. Doctor
   B. Coal Miner
   C. Businessman
   D. Shoe maker

4.) Which vice-president of the United States was a pharmacist?
   A. Hubert Humphrey
   B. Dan Quayle
   C. Nelson Rockefeller
   D. Charles Curtis

5.) Which of the following did NOT have a job related to pharmacy?
   A. Agatha Christie
   B. Edgar Allen Poe
   C. Dante Alighieri
   D. Sir Isaac Newton
   E. Benjamin Franklin

Pharmacy Pick Up Lines

Just in Time for Valentine's Day!

- Are you a box of BD Pen needles? Because you are ultra-fine!
- I think you're suffering from a lack of Vitamin Me
- Excuse me, do you have a chewable aspirin? I just got chest pain when I laid eyes on you
- Just call me Lasix, 'cause I'll keep you up all night
- My love for you is like diarrhea- I can't hold it in
- With you around sweetie, who needs glucose tablets?
- I wish I was your coronary artery, so I could be wrapped around your heart
- Excuse me, do you have any albuterol? You just took my breath away
- I wish I was adenine, then I could be paired with U
- I'm like morphine, I'll make sure all your pains go away when you're with me
- You're so pharma-cute-ical
- Even Pepcid AC can't stop my heart burning for you

Answers: 1.) C 2.) B 3.) D 4.) A 5.) B